



## Clinical trial results:

### A Phase 2, Single-arm, Pathologist-blinded Study Using Liver Biopsy Specimens to Assess Copper Concentration and Histopathologic Changes in Patients with Wilson Disease who are Treated with ALXN1840 for 48 Weeks Followed by an Extension Treatment Period with ALXN1840 for up to an Additional 48 Weeks

#### Summary

EudraCT number	2019-003711-60
Trial protocol	DE BE DK GB FR AT
Global end of trial date	13 June 2023

#### Results information

Result version number	v1 (current)
This version publication date	26 May 2024
First version publication date	26 May 2024

#### Trial information

##### Trial identification

Sponsor protocol code	ALXN1840-WD-205
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04422431
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Alexion Pharmaceuticals, Inc.
Sponsor organisation address	121 Seaport Boulevard, Boston, MA, United States, 02210
Public contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc., +35 3874162507, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc., +35 3874162507, clinicaltrials.eu@alexion.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 June 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 June 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate change in liver copper concentration following treatment with ALXN1840 at Week 48 in participants with Wilson disease (WD).

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
- Applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) -Good Clinical Practice (GCP) Guidelines
- Applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 9
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Singapore: 2
Worldwide total number of subjects	31
EEA total number of subjects	6

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	28
From 65 to 84 years	3
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study included a screening period of up to 4 weeks.

### Period 1

Period 1 title	Treatment Period (48 Weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	ALXN1840
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Arm description:

Participants received ALXN1840 orally in the 48-week Treatment Period. Participants who completed the 48-week Treatment Period and agreed to enter a 48-week Extension Period, continued to receive ALXN1840. Participants who did not enter the Extension Period discontinued dosing at Week 48, and had a final study visit for safety follow-up at Week 52.

Arm type	Experimental
Investigational medicinal product name	ALXN1840
Investigational medicinal product code	
Other name	WTX101 (former name)
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage and administration details as described in the arm description.

Number of subjects in period 1	ALXN1840
Started	31
Received at least 1 dose of study drug	31
Completed	26
Not completed	5
Consent withdrawn by subject	1
Adverse event, non-fatal	3
Other than specified	1

**Period 2**

Period 2 title	Extension Period (48 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

**Arms**

<b>Arm title</b>	ALXN1840
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## Arm description:

Participants received ALXN1840 orally in the 48-week Treatment Period. Participants who completed the 48-week Treatment Period and agreed to enter a 48-week Extension Period, continued to receive ALXN1840. Participants who did not enter the Extension Period discontinued dosing at Week 48, and had a final study visit for safety follow-up at Week 52.

Arm type	Experimental
Investigational medicinal product name	ALXN1840
Investigational medicinal product code	
Other name	WTX101 (former name)
Pharmaceutical forms	Tablet
Routes of administration	Oral use

## Dosage and administration details:

Dosage and administration details as described in the arm description.

<b>Number of subjects in period 2<sup>[1]</sup></b>	ALXN1840
Started	25
Received at least 1 dose of study drug	25
Completed	21
Not completed	4
Consent withdrawn by subject	1
Other than specified	2
Lost to follow-up	1

## Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 1 participant completed the Treatment Period, but did not enter the Extension Period.

## Baseline characteristics

### Reporting groups

Reporting group title	ALXN1840
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Reporting group description:

Participants received ALXN1840 orally in the 48-week Treatment Period. Participants who completed the 48-week Treatment Period and agreed to enter a 48-week Extension Period, continued to receive ALXN1840. Participants who did not enter the Extension Period discontinued dosing at Week 48, and had a final study visit for safety follow-up at Week 52.

Reporting group values	ALXN1840	Total	
Number of subjects	31	31	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	28	28	
From 65-84 years	3	3	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	38.8		
standard deviation	± 14.47	-	
Sex: Female, Male			
Units: participants			
Female	11	11	
Male	20	20	
Race			
Units: Subjects			
American Indian/Alaska Native	0	0	
Asian	6	6	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
White	21	21	
Other	3	3	
Unknown	1	1	
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	25	25	
Not Reported	3	3	
Unknown	1	1	

## End points

### End points reporting groups

Reporting group title	ALXN1840
Reporting group description: Participants received ALXN1840 orally in the 48-week Treatment Period. Participants who completed the 48-week Treatment Period and agreed to enter a 48-week Extension Period, continued to receive ALXN1840. Participants who did not enter the Extension Period discontinued dosing at Week 48, and had a final study visit for safety follow-up at Week 52.	
Reporting group title	ALXN1840
Reporting group description: Participants received ALXN1840 orally in the 48-week Treatment Period. Participants who completed the 48-week Treatment Period and agreed to enter a 48-week Extension Period, continued to receive ALXN1840. Participants who did not enter the Extension Period discontinued dosing at Week 48, and had a final study visit for safety follow-up at Week 52.	

### Primary: Change From Baseline in Liver Cu Concentration at Week 48 (Treatment Period)

End point title	Change From Baseline in Liver Cu Concentration at Week 48 (Treatment Period) <sup>[1]</sup>
End point description: Liver biopsy samples were taken for the assessment of liver Cu concentration. Multiple imputation was used to impute missing data at Week 48 due to any reason based on Baseline values. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable.	
End point type	Primary
End point timeframe: Baseline, Week 48 (Treatment Period)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Due to limitations of the EudraCT system, statistical analysis could not be provided for a single reporting group.	

End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: µg/g				
arithmetic mean (standard error)	92.8 (± 56.34)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Change From Baseline in Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Fibrosis Stage at Week 48 (Treatment Period)

End point title	Number of Participants With Change From Baseline in Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Fibrosis Stage at Week 48 (Treatment Period)
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**End point description:**

Fibrosis from histology was evaluated by NASH CRN Fibrosis Stage, which was scaled from 0 to 4 stages where Score 0: None; Score 1: Perisinusoidal or periportal - 1a - mild, zone 3, perisinusoidal; Score 1: Perisinusoidal or periportal - 1b - moderate, zone 3, perisinusoidal; Score 1: Perisinusoidal or periportal - 1c - portal/periportal; Score 2: Both perisinusoidal and portal/periportal; Score 3: Bridging fibrosis; and Score 4: Cirrhosis. Higher scores indicated greater fibrosis. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Number analyzed' signifies participants evaluable at specified timepoint.

End point type	Secondary
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**End point timeframe:**

Baseline, Week 48 (Treatment Period)

End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: participants				
Baseline Score 0	7			
Baseline Score 1a	1			
Baseline Score 1b	0			
Baseline Score 1c	7			
Baseline Score 2	3			
Baseline Score 3	8			
Baseline Score 4	2			
Baseline Not Evaluable	1			
Week 48 Score 0	5			
Week 48 Score 1a	0			
Week 48 Score 1b	0			
Week 48 Score 1c	6			
Week 48 Score 2	6			
Week 48 Score 3	7			
Week 48 Score 4	0			
Week 48 Not Evaluable	0			

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Participants With Change From Baseline in Metavir Fibrosis Score at Week 48 (Treatment Period)**

End point title	Number of Participants With Change From Baseline in Metavir Fibrosis Score at Week 48 (Treatment Period)
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**End point description:**

Fibrosis from histology was evaluated by Metavir Fibrosis Score, which was ranged from 0 to 4 where Score 0: No fibrosis; Score 1: Stellate enlargement of portal tract but without septa formation; Score 2: Enlargement of portal tract with rare septa formation; Score 3: Numerous septa without cirrhosis; and Score 4: Cirrhosis. Higher scores indicated greater fibrosis. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Number analyzed' signifies participants evaluable at specified timepoint.



End point type	Secondary
End point timeframe:	
Baseline, Week 48 (Treatment Period)	

End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: participants				
Baseline Score 0	8			
Baseline Score 1	7			
Baseline Score 2	4			
Baseline Score 3	7			
Baseline Score 4	2			
Baseline Not Evaluable	1			
Week 48 Score 0	5			
Week 48 Score 1	4			
Week 48 Score 2	8			
Week 48 Score 3	7			
Week 48 Score 4	0			
Week 48 Not Evaluable	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Change From Baseline in Ishak Fibrosis Score at Week 48 (Treatment Period)

End point title	Number of Participants With Change From Baseline in Ishak Fibrosis Score at Week 48 (Treatment Period)
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End point description:

Fibrosis from histology was evaluated by Ishak Fibrosis Score, which was ranged from 0 to 6 where Score 0: No fibrosis; Score 1: Fibrous expansion of some portal areas, with or without short fibrous septa; Score 2: Fibrous expansion of most portal areas, with or without short fibrous septa; Score 3: Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging; and Score 4: Fibrous expansion of portal areas with marked bridging (P-P) as well as portal central (P-C); Score 5: Marked bridging (P-P and/or P-C) with occasional nodules (incomplete cirrhosis); and Score 6: Cirrhosis, probable or definite. Higher scores indicated greater fibrosis. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Number analyzed' signifies participants evaluable at specified timepoint.

End point type	Secondary
End point timeframe:	
Baseline, Week 48 (Treatment Period)	

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: participants				
Baseline Score 0	8			
Baseline Score 1	6			
Baseline Score 2	2			
Baseline Score 3	9			
Baseline Score 4	1			
Baseline Score 5	1			
Baseline Score 6	1			
Baseline Not Evaluable	1			
Week 48 Score 0	5			
Week 48 Score 1	4			
Week 48 Score 2	4			
Week 48 Score 3	8			
Week 48 Score 4	3			
Week 48 Score 5	0			
Week 48 Score 6	0			
Week 48 Not Evaluable	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Hepatic Collagen Content at Week 48 (Treatment Period)

End point title	Change From Baseline in Hepatic Collagen Content at Week 48 (Treatment Period)
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End point description:

Fibrosis from histology was evaluated by morphometric quantification of hepatic collagen content. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 48 (Treatment Period)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: percentage of collagen				
arithmetic mean (standard deviation)	8.5445 (± 15.54224)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in a-SMA Content at Week 48 (Treatment Period)

End point title	Change From Baseline in a-SMA Content at Week 48 (Treatment Period)
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End point description:

Fibrosis from histology was evaluated by morphometric quantification of hepatic a-SMA content. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 48 (Treatment Period)

End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: percentage of a-SMA				
arithmetic mean (standard deviation)	1.6002 ( $\pm$ 5.47274)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Change From Baseline in NAS Steatosis Grading Score at Week 48 (Treatment Period)

End point title	Number of Participants With Change From Baseline in NAS Steatosis Grading Score at Week 48 (Treatment Period)
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End point description:

Steatosis from histology was evaluated by the steatosis component of the NAS, which was ranged from 0 to 3 where Score 0: < 5% (minimal); Score 1: 5 - 33% (mild); Score 2: 34 - 66% (moderate); and Score 3: > 66% (severe). Higher scores indicated greater steatosis. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Number analyzed' signifies participants evaluable at specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 48 (Treatment Period)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: participants				
Baseline Score 0	19			
Baseline Score 1	6			
Baseline Score 2	3			
Baseline Score 3	1			
Week 48 Score 0	15			
Week 48 Score 1	6			
Week 48 Score 2	2			
Week 48 Score 3	1			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Hepatic Fat Content at Week 48 (Treatment Period)

End point title	Change From Baseline in Hepatic Fat Content at Week 48 (Treatment Period)
End point description:	
Steatosis from histology was evaluated by morphometric quantification of hepatic fat content. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.	
End point type	Secondary
End point timeframe:	
Baseline, Week 48 (Treatment Period)	

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: percentage of fat				
arithmetic mean (standard deviation)	-0.2504 ( $\pm$ 2.19263)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Extension Period: Number of Participants With TEAEs

End point title	Extension Period: Number of Participants With TEAEs
End point description:	
An AE was defined as any untoward medical occurrence associated with the use of a drug in humans,	

whether or not considered drug related. An SAE was an AE that met at least 1 of the following criteria: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization for the AE, persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, congenital anomaly/birth defect (in the child of a participant who was exposed to the study drug), important medical event or reaction. The TEAEs were AEs with onset on or after the first study drug dose. A summary of all Serious Adverse Events and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety Analysis Set in the Extension Period included all participants who received at least 1 dose of ALXN1840 in the Extension Period.

End point type	Secondary
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End point timeframe:

Day 1 (Extension Period) up Week 52 (Extension Period)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: participants	24			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Treatment Period: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Treatment Period: Number of Participants With Treatment-emergent Adverse Events (TEAEs)
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End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An SAE was an AE that met at least 1 of the following criteria: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization for the AE, persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, congenital anomaly/birth defect (in the child of a participant who was exposed to the study drug), important medical event or reaction. The TEAEs were AEs with onset on or after the first study drug dose. A summary of all Serious Adverse Events and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety Analysis Set in the Treatment Period included all participants who received at least 1 dose of treatment in the Treatment Period.

End point type	Secondary
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End point timeframe:

Day 1 (Treatment Period) up to Week 48 (Treatment Period)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: participants	30			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in NAS Total Score at Week 48 (Treatment Period)

End point title	Change From Baseline in NAS Total Score at Week 48 (Treatment Period)
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End point description:

Inflammation was quantified by the NAS total score. The score is defined as the unweighted sum of the scores for steatosis (0 [minimal] to 3 [severe]), lobular inflammation (0 [none] to 3 [ $>4$  foci / 200x field]), and hepatocellular ballooning (0 [none] to 2 [many]), thus ranging from 0 (no inflammation) to 8 (severe inflammation), with higher scores indicating more severe disease. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 48 (Treatment Period)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: units on a scale				
arithmetic mean (standard deviation)	0.1 ( $\pm$ 1.69)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Treatment Period: Predose Trough Plasma Total Mo Concentration

End point title	Treatment Period: Predose Trough Plasma Total Mo Concentration
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End point description:

Pharmacokinetic (PK) Analysis Set in the Treatment Period included all participants who received at least 1 dose of treatment in the Treatment Period and had evaluable PK data for total Mo and/or plasma ultrafiltrate (PUF) Mo (as surrogate measure for ALXN1840 PK) in plasma in the Treatment Period. 'Overall number of participants analyzed' = participants evaluable for this outcome measure. 'Number analyzed' = participants evaluable at specified timepoint.

End point type	Secondary
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End point timeframe:

Predose up to 4 hours postdose at Week 6 (Day 43) and Week 36 (Day 253)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: nanograms (ng)/milliliter (mL)				
arithmetic mean (standard deviation)				
Week 6	174.39 ( $\pm$ 113.824)			
Week 36	131.19 ( $\pm$ 103.359)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical Global Impression-Improvement (CGI-I) Scale Score at Week 48 (Treatment Period)

End point title	Clinical Global Impression-Improvement (CGI-I) Scale Score at Week 48 (Treatment Period)
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End point description:

The CGI-I is a 7-point scale clinician assessment where 1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; or 7 = very much worse. Higher scores indicated worsening of disease. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Week 48 (Treatment Period)

<b>End point values</b>	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	3.1 ( $\pm$ 1.26)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Mo in Liver Biopsy Specimen at Week 48 (Treatment Period)

End point title	Change From Baseline in Mo in Liver Biopsy Specimen at Week
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## End point description:

The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary
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## End point timeframe:

Baseline, Week 48 (Treatment Period)
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End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: µg/g				
arithmetic mean (standard deviation)	69.6976 (± 43.02655)			

## Statistical analyses

No statistical analyses for this end point

**Secondary: Treatment Period: Predose Trough Plasma Total PUF Mo Concentration**

End point title	Treatment Period: Predose Trough Plasma Total PUF Mo Concentration
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## End point description:

PK Analysis Set in the Treatment Period included all participants who received at least 1 dose of treatment in the Treatment Period and had evaluable PK data for total Mo and/or PUF Mo (as surrogate measure for ALXN1840 PK) in plasma in the Treatment Period. 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
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## End point timeframe:

Predose up to 4 hours postdose at Week 6 (Day 43) and Week 36 (Day 253)
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End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 6	5.888 (± 2.0176)			
Week 36	7.843 (± 6.0564)			



## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in CGI-S Scale Score at Week 48 (Treatment Period)

End point title	Change From Baseline in CGI-S Scale Score at Week 48 (Treatment Period)
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End point description:

The CGI-S is a 7-point scale clinician assessment. Participants were assessed on severity of illness at the time of rating/assessment as follows: 1 = normal, not at all ill; 2 = borderline ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; or 7 = extremely ill. Higher scores indicated worsening of disease. The Full Analysis Set in the Treatment Period included all participants who received at least 1 dose of study drug in the Treatment Period and had at least a Baseline liver Cu value evaluable. 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 48 (Treatment Period)

End point values	ALXN1840			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.4 (± 1.50)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 (Treatment Period) up to Week 52 (Extension Period) (up to a total of approximately 100 weeks)

Adverse event reporting additional description:

Serious and other adverse events are reported in the Safety Analysis Set in the Treatment Period (all participants who received at least 1 dose of treatment in the Treatment Period), and for the Safety Analysis Set in the Extension Period, (all participants who received at least 1 dose of ALXN1840 in the Extension Period).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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### Reporting groups

Reporting group title	Treatment Period: ALXN1840
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Reporting group description:

Participants received ALXN1840 orally in the 48-week Treatment Period.

Reporting group title	Extension Period: ALXN1840
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Reporting group description:

Participants who completed the 48-week Treatment Period and agreed to enter a 48-week Extension Period, continued to receive ALXN1840.

Serious adverse events	Treatment Period: ALXN1840	Extension Period: ALXN1840	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 31 (9.68%)	2 / 25 (8.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			

subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatobiliary disorders</b>			
Drug-induced liver injury			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal and urinary disorders</b>			
Bence Jones proteinuria			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Psychiatric disorders</b>			
Suicidal ideation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Treatment Period: ALXN1840	Extension Period: ALXN1840	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 31 (96.77%)	24 / 25 (96.00%)	
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
Seborrhoeic keratosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			

subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 31 (16.13%)	3 / 25 (12.00%)	
occurrences (all)	6	3	
Fatigue			
subjects affected / exposed	4 / 31 (12.90%)	2 / 25 (8.00%)	
occurrences (all)	4	2	
Asthenia			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Chills			
subjects affected / exposed	2 / 31 (6.45%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Generalised oedema			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Feeling abnormal			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Temperature intolerance			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Swelling			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Influenza like illness			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	
occurrences (all)	2	3	
Immunisation reaction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	4	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Breast tenderness			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Dysmenorrhoea	Additional description: The N at risk for this adverse event has been adjusted to the number of females in the respective study periods as it is a sex-specific event.		
subjects affected / exposed <sup>[1]</sup>	1 / 11 (9.09%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Haemorrhagic ovarian cyst	Additional description: The N at risk for this adverse event has been adjusted to the number of females in the respective study periods as it is a sex-specific event.		
subjects affected / exposed <sup>[2]</sup>	1 / 11 (9.09%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Heavy menstrual bleeding	Additional description: The N at risk for this adverse event has been adjusted to the number of females in the respective study periods as it is a sex-specific event.		
subjects affected / exposed <sup>[3]</sup>	1 / 11 (9.09%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Respiratory disorder			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Rhinorrhoea			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Nasal septum deviation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory symptom			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	2	
Depressed mood			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	

Depression			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 31 (3.23%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Personality disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 31 (3.23%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Suicidal ideation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Investigations			
Protein urine present			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	8 / 31 (25.81%)	8 / 25 (32.00%)	
occurrences (all)	9	9	
Gamma-glutamyltransferase increased			
subjects affected / exposed	8 / 31 (25.81%)	7 / 25 (28.00%)	
occurrences (all)	8	8	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 31 (12.90%)	4 / 25 (16.00%)	
occurrences (all)	4	4	
Hepatic enzyme increased			
subjects affected / exposed	4 / 31 (12.90%)	2 / 25 (8.00%)	
occurrences (all)	5	2	
Aspartate aminotransferase increased			

subjects affected / exposed	3 / 31 (9.68%)	2 / 25 (8.00%)
occurrences (all)	3	2
Blood creatine phosphokinase increased		
subjects affected / exposed	3 / 31 (9.68%)	4 / 25 (16.00%)
occurrences (all)	3	5
Transaminases increased		
subjects affected / exposed	3 / 31 (9.68%)	2 / 25 (8.00%)
occurrences (all)	3	2
Blood bilirubin increased		
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)
occurrences (all)	3	1
Liver function test increased		
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)
occurrences (all)	2	2
Alanine aminotransferase abnormal		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Blood albumin decreased		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0
Blood folate decreased		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Creatinine renal clearance decreased		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0
Creatinine renal clearance increased		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Prothrombin time prolonged		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0
Urobilinogen urine increased		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0



Weight decreased subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Weight increased subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Urine analysis abnormal subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Head injury subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Ligament sprain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Post procedural fever subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	0 / 25 (0.00%) 0	
Post procedural haematuria subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Post procedural hypotension subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Post procedural swelling subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Post vaccination syndrome			

subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Road traffic accident			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Upper limb fracture			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Incision site pain			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Neck injury			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Procedural complication			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Rib fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 31 (22.58%)	6 / 25 (24.00%)	
occurrences (all)	9	8	
Lethargy			
subjects affected / exposed	3 / 31 (9.68%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Dizziness			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	
occurrences (all)	2	2	

Presyncope			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Tremor			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Paraesthesia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Balance disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Serotonin syndrome			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Leukopenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 31 (6.45%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Ear pain			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 25 (8.00%) 2	
Vertigo subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Eye disorders			
Vitreous detachment subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Vision blurred subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	0 / 25 (0.00%) 0	
Chalazion subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Myopia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 6	6 / 25 (24.00%) 7	
Abdominal pain subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	2 / 25 (8.00%) 2	
Abdominal discomfort subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	3 / 25 (12.00%) 3	
Haemorrhoids thrombosed subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Mouth ulceration subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	1 / 25 (4.00%) 2	
Toothache			

subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	1 / 31 (3.23%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Faeces discoloured			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 31 (3.23%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Dry mouth			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Oral pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	
occurrences (all)	2	2	
Constipation			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Hepatobiliary disorders			

Hypertransaminasaemia subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	2 / 25 (8.00%) 3	
Skin and subcutaneous tissue disorders			
Diabetic foot subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	2 / 25 (8.00%) 3	
Pruritus subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Idiopathic guttate hypomelanosis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Erythema subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Ingrown hair subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Glycosuria subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 25 (0.00%) 0	
Proteinuria subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 25 (4.00%) 1	
Haematuria			

subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 31 (9.68%)	4 / 25 (16.00%)	
occurrences (all)	4	5	
Back pain			
subjects affected / exposed	1 / 31 (3.23%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Greater trochanteric pain syndrome			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Joint effusion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Back disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Axillary mass			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Muscular weakness			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 25 (4.00%) 1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 31 (16.13%)	8 / 25 (32.00%)	
occurrences (all)	5	10	
COVID-19			
subjects affected / exposed	4 / 31 (12.90%)	10 / 25 (40.00%)	
occurrences (all)	4	10	
Kidney infection			
subjects affected / exposed	2 / 31 (6.45%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 31 (6.45%)	4 / 25 (16.00%)	
occurrences (all)	2	7	
Urinary tract infection			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	
occurrences (all)	4	1	
Bacterial vaginosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Dermatophytosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Folliculitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Furuncle			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	



Gingivitis		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Helicobacter infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0
Lower respiratory tract infection		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Paronychia		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Post procedural sepsis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0
Respiratory tract infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)
occurrences (all)	1	0
Sinusitis		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	2
Respiratory tract infection viral		
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)
occurrences (all)	1	1
Bacteriuria		
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	1
Rhinitis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	1
Gastroenteritis		
subjects affected / exposed	0 / 31 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	2
Viral upper respiratory tract infection		
subjects affected / exposed	0 / 31 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	3

Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	3 / 31 (9.68%)	3 / 25 (12.00%)	
occurrences (all)	3	3	
Decreased appetite			
subjects affected / exposed	2 / 31 (6.45%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Diabetes mellitus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Dyslipidaemia			
subjects affected / exposed	1 / 31 (3.23%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Hyperglycaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Hyponatraemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Iron deficiency			
subjects affected / exposed	1 / 31 (3.23%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Hyperlipidaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 31 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The N at risk for this adverse event has been adjusted to the number of females in the respective study periods as it is a sex-specific event.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The N at risk for this adverse event has been adjusted to the number of females in the

respective study periods as it is a sex-specific event.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The N at risk for this adverse event has been adjusted to the number of females in the respective study periods as it is a sex-specific event.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2020	Addition of the requirement for Alexion approval prior to increasing the dose of ALXN1840. Administrative Change Letters since approval of the previous protocol were also incorporated.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported